

## INTERNATIONAL SEARCH REPORT

International application No

PCT/US04/33091

<b>A CLASSIFICATION OF SUBJECT MATTER</b> IPC C12N 5/06( 2006 01),5/08( 2006 01)  USPC 435/370 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B FIELDS SEARCHED</b>  Minimum documentation searched (classification system followed by classification symbols) US 435/370  Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet		
<b>C DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X --- Y	US 5,665,589 (HARRIS et al) 9 September 1997 (09 09 1997), abstract, column 2, lines 16-25 column 3, lines 9, 13 and 24, column 4, lines 16 and 36, column 7, lines 43-67	1-8,12-21, 23-25,28,30 ----- 9-1 1,22,26,27,29,31-34
X --- Y	US 6,107,043 (JAUREGUI ET LA) 22 August 2000 (22 08 2000), abstract, column 3, lines 51-65, column 8, lines 58-67, column 11, lines 48-56	1,4-8,12-22,30 ----- 2,3,9-1 1,23-29,31-34
X --- Y	MILLS et al Induction of drug metabolism enzymes and MDRI using a novel human hepatocyte cell line Journal of Pharmacology and Experimental Therapeutics April 2004, Vol 309 No 1, pages 303-309, especially abstract	1-31, 33 ----- 32, 34
Y	US 6,653,105 B2 (TRGLIA et al) 25 November 2003 (25 22 2005), column 2, lines 40-50, column 7, lines 1-15, column 8, line 20, column 9, lines 17-34, column 10, lines 27-32	1-34
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <b>Ü</b> See patent family annex		
* Special categories of cited documents A document defining the general state of the art which is not considered to be of particular relevance E earlier application or patent published on or after the international filing date I document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) O document referring to an oral disclosure use exhibition or other means P document published prior to the international filing date but later than the priority date claimed T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention X document of particular relevance the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone Y document of particular relevance the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents such combination being obvious to a person skilled in the art & document member of the same patent family		
Date of the actual completion of the international search 01 March 2006 (01 03 2006)		Date of mailing of the international search report 24 MAR 2006
Name and mailing address of the ISA/US Mail Stop PCT, Attn ISA/US Commissioner for Patents P O Box 1450 Alexandria, Virginia 22313-1450 Facsimile No (571) 273-3201		Authorized officer Vera Afremova Telephone No (571) 272-1600

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**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons

- 1 ☐ Claims Nos  
because they relate to subject matter not required to be searched by this Authority, namely
- 2 ☐ Claims Nos  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically
- 3 ☐ Claims Nos  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 64(a)

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

Oiled International Searching Authority found multiple inventions in this international application as follows  
Please See Continuation Sheet

- 1 ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
- 2 ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees
- 3 ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos
- 4 ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims, it is covered by claims Nos 1-34
- Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation
- ☐ No protest accompanied the payment of additional search fees

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**BOX III OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-34, drawn to a virally-immortalized hepatocyte

Group II, claim(s) 35-40, drawn to a first method of using a virally-immortalized hepatocyte for accessing effects of a chemical entity on a liver

Group III, claim(s) 41-45, drawn to a second method of using a virally-immortalized hepatocyte for accessing enzyme induction

Group IV, claim(s) 46-50, drawn to a third method of using a virally-immortalized hepatocyte for accessing cellular toxicity

Group V, claim(s) 51-57, drawn to a fourth method of using a virally-immortalized hepatocyte for accessing effects of a liver on a chemical entity

Group VI, claim(s) 58, drawn to 22 various assays procedures wherein each procedure is relied upon on the use of a virally-immortalized hepatocyte

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:  
the species are different assays 1 through 22 as recited in claim 58.  
The following claim(s) are/is generic: 58.

The inventions listed as the Groups I through VI and the species 1 through 22 within the Group VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature such as a virally-immortalized hepatocyte is known in the prior art. For example, US 6,107,043 and US 6,046,050 disclose virally-immortalized hepatocytes that are derived from normal liver cells, non-tumorigenic and have normal metabolic activity and/or produce plasma proteins (see abstracts).

Thus, the corresponding special technical feature is known and, therefore, unity of inventions is broken.

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Continuation of B FIELDS SEARCHED Item 3

WEST USPT, PGPUB, STN BIOSIS, NEDLINE,

search terra immortalized hepatic cells, nontumorigenic, SV40 TAG, nontumoP450, plasma proteins, albumin, antitrypsin, transferrin, clotting factors, drug testing

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